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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 02	STN pricing information for 2008 now available
NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
NEWS	10	FEB 20	PCI now available as a replacement to DPCI
NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUIDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAPplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements
NEWS	23	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS	24	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	25	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	26	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	27	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	28	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS	29	JUN 25	CA/CAPplus and USPAT databases updated with IPC reclassification data
NEWS	30	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records

NEWS 31 JUN 30 EMBASE, EMBAL, and LEMBASE updated with additional
options to display authors and affiliated
organizations
NEWS 32 JUN 30 STN on the Web enhanced with new STN AnaVist
Assistant and BLAST plug-in
NEWS 33 JUN 30 STN AnaVist enhanced with database content from EPFULL

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:49:38 ON 25 JUL 2008

=> file caplus

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FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 15:50:17 ON 25 JUL 2008

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FILE COVERS 1907 - 25 Jul 2008 VOL 149 ISS 5
FILE LAST UPDATED: 24 Jul 2008 (20080724/ED)

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They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

=> e hergenrother p/au

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E1      7      HERGENROTHER K M/AU
E2      6      HERGENROTHER KARL M/AU
E3      0 --> HERGENROTHER P/AU
E4      171     HERGENROTHER P M/AU
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E12     1      HERGENROTHER R W/AU

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=> s e4-e10

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      M"/AU)

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=> e putt k/au

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E6      18     PUTT KARSON S/AU
E7      1      PUTT KARSON STACKHOUSE/AU
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E10     7      PUTT M S/AU
E11     18     PUTT MARK S/AU
E12     10     PUTT MARY/AU

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=> s e4-e7

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=> l1 or l2

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L3      385 L1 OR L2

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=> l3 and (nad or nadh)

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      42465 NAD
      229 NADS
      42670 NAD
      (NAD OR NADS)
      40788 NADH
      2 NADHS
      40788 NADH
      (NADH OR NADHS)

```

L4 7 L3 AND (NAD OR NADH)

=> d l4 1-7 ibib abs

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1388745 CAPLUS
DOCUMENT NUMBER: 148:185178
TITLE: Poly(ADP-ribose) makes a date with death
AUTHOR(S): Heeres, James T.; Hergenrother, Paul J.
CORPORATE SOURCE: Department of Chemistry, Roger Adams Laboratory,
University of Illinois, Urbana, IL, 61801, USA
SOURCE: Current Opinion in Chemical Biology (2007), 11(6),
644-653
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Poly(ADP-ribose) polymerase (PARP) catalyzes the conversion of NAD to polymers of poly(ADP-ribose) (PAR). Although its role in the DNA-damage response has long been recognized, recent work indicates that PAR itself acts at mitochondria to directly induce cell death through stimulation of apoptosis-inducing factor (AIF) release. Here, the authors discuss PAR synthesis and degradation, and the role of PAR misregulation in various disease states. Attention is given to opportunities for therapeutic intervention with small mols. that are involved in PAR signaling, with specific focus on poly(ADP-ribose) glycohydrolase (PARG) and AIF.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1000111 CAPLUS
DOCUMENT NUMBER: 148:281807
TITLE: Increased poly(ADP-ribose) polymerase activity during porcine hemorrhagic shock is transient and predictive of mortality
AUTHOR(S): Skarda, David E.; Putt, Karson S.;
Hergenrother, Paul J.; Mulier, Kristine E.;
Beilman, Greg J.
CORPORATE SOURCE: Department of Surgery, University of Minnesota,
Minneapolis, MN, 55433, USA
SOURCE: Resuscitation (2007), 75(1), 135-144
CODEN: RSUSBS; ISSN: 0300-9572
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aim of the study: The aim of our study was to compare poly(ADP-ribose) polymerase (PARP) activity levels in a porcine model of hemorrhagic shock and resuscitation. Materials and methods: We designed a prospective, comparative randomized survival study of hemorrhagic shock using 20 male Yorkshire-Landrace pigs (15-25 kg). In 16 pigs after splenectomy, we induced hemorrhagic shock to a mean arterial pressure of 50 mm Hg (.apprx.35% bleed). Pigs were randomized to receive normotensive resuscitation (SBP 90 mm Hg), mild hypotensive resuscitation (SBP 80 mm Hg), moderate hypotensive resuscitation (SBP 65 mm Hg), or no resuscitation (n = 4 in each group). We also included a group of sham animals that were instrumented and had a splenectomy but not bled (n = 4). Muscle and liver biopsies were taken prior to hemorrhage, after 45 min of shock, and 8, 24, and 48 h after resuscitation. PARP activity levels in biopsies were measured using chemical quantitation of NAD+.

Results: Irresp. of our resuscitation strategy or outcome, both muscle and liver PARP activity levels rose after 45 min of shock and then returned to baseline. Excluding our control animals, PARP activity levels were significantly higher during shock in non-survivors compared to survivors. Conclusions: In our model of porcine hemorrhagic shock, PARP activity levels increased during hemorrhagic shock. However, this increase in PARP activity levels was transient as they returned to baseline regardless of resuscitation strategy. Interestingly, PARP activity levels were significantly higher during hemorrhagic shock in non-survivors compared to survivors. These findings suggest that PARP activity may be a part of initial pathways leading from hemorrhagic shock to death.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:356589 CAPLUS

DOCUMENT NUMBER: 147:25773

TITLE: A colorimetric substrate for poly(ADP-ribose) polymerase-1, VPARP, and tankyrase-1

AUTHOR(S): Nottbohm, Amanda C.; Dothager, Robin S.; Putt, Karson S.; Hoyt, Mirth T.; Hergenrother, Paul J.

CORPORATE SOURCE: Department of Chemistry, University of Illinois, Urbana, IL, 61801, USA

SOURCE: Angewandte Chemie, International Edition (2007), 46(12), 2066-2069

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Poly(ADP-ribose) polymerases (PARPs) play a major role in cellular survival and maintenance of energy stores after genotoxic insult. The colorimetric PARP substrate ADP-ribose-PNP can be used to monitor PARP activity. By monitoring the production of p-nitrophenolate, the kinetic parameters of PARP-1, tankyrase-1, and PARP-4 could be evaluated.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:113734 CAPLUS

DOCUMENT NUMBER: 146:206321

TITLE: Pyridazine compounds as PARG and/or PARP inhibitors and their preparation, pharmaceutical compositions, and use for the treatment of neurodegeneration and stroke

INVENTOR(S): Hergenrother, Paul J.; Putt, Karson S.; Liu, Xianjun

PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA

SOURCE: PCT Int. Appl., 109pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

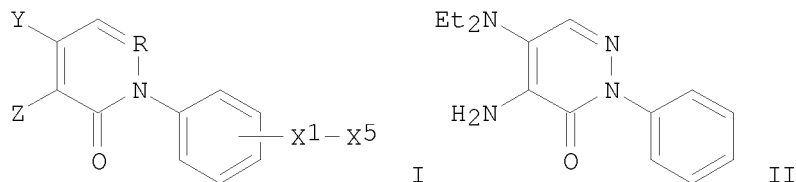
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014226	A2	20070201	WO 2006-US28894	20060726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20070032496 A1 20070208 US 2006-460073 20060726
 PRIORITY APPLN. INFO.: US 2005-702445P P 20050726
 OTHER SOURCE(S): MARPAT 146:206321
 GI



AB Compds. of formula I and related methods for synthesis, and the use of compds. for the treatment of neurodegenerative diseases are disclosed. Compds. of formula I wherein R is C or N; Y is NH₂ and derivs., halo, and acyl; Z is NH₂ and derivs., halo, and a group that can be converted to NH₂ under physiol. conditions; X₁ - X₅ is H, halo, alkyl, alkyl halide, OH, OMe, and alkoxy; are claimed. Compds. of formula I are disclosed in connection with PARG and/or PARP inhibition. Therapeutic applications are relevant for preventing or inhibiting neurol. cell death for a variety of neurodegenerative conditions including Parkinson's disease, ischemia, and stroke. Also disclosed is a high-throughput screen for identifying compds. capable of inhibiting PARG and/or PARP. Example compound II was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their PARG and/or PARP inhibitory activity. From the assay, it was determined that compound II exhibited good PARG inhibitory activity.

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:856685 CAPLUS
 TITLE: Development and application of the first colorimetric poly(ADP-ribose)polymerase (PARP) substrate
 AUTHOR(S): Nottbohm, Amanda C.; Dothager, Robin S.; Putt, Karson S.; Hoyt, Mirth; Hergenrother, Paul J.
 CORPORATE SOURCE: Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL, 61801, USA
 SOURCE: Abstracts of Papers, 232nd ACS National Meeting, San Francisco, CA, United States, Sept. 10-14, 2006 (2006), BIOL-206. American Chemical Society: Washington, D. C.
 CODEN: 69IHRD
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)

LANGUAGE: English

AB Utilizing β - NAD⁺ to catalyze the synthesis of ADP-ribose polymers onto a variety of protein acceptors, the poly(ADP-ribose) polymerase (PARP) family of enzymes is involved in countless cellular functions. As PARPs play a critical role in cellular survival and maintenance of energy stores after genotoxic insult, small mol. inhibitors of PARP isoenzymes have been touted as possible therapies for neurodegeneration, ischemia, and as potentiators of anticancer therapies. Current methods for measuring PARP activity are inconvenient and low throughput; thus neither direct kinetic comparison of PARP isoenzyme activities nor IC50 comparison of known PARP inhibitors against the multitude of PARP isoenzymes has been offered in the literature. We have therefore developed an assay which utilizes a colorimetric PARP substrate to kinetically monitor PARP activity. By employing this new substrate, we have determined kinetic parameters of PARP-1, tankyrase, and VPARP, and these results offer insight into the isoenzyme specificity of known PARP inhibitors.

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:371413 CAPLUS

DOCUMENT NUMBER: 142:406532

TITLE: Fluorescent derivative of NAD in methods of detecting poly(ADP-ribose) polymerase and other NAD-utilizing enzymes

INVENTOR(S): Hergenrother, Paul J.; Putt, Karson S.

PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005038043	A2	20050428	WO 2004-US34010	20041014
WO 2005038043	A3	20050707		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20070078100	A1	20070405	US 2006-595360	20061221
PRIORITY APPLN. INFO.:			US 2003-510916P	P 20031014
			WO 2004-US34010	W 20041014

AB The present invention makes use of the discovery that poly(ADP-ribose) polymerase (PARP) and other NAD-utilizing enzymes can be readily detected using a highly sensitive, convenient, simple assay that relies upon the chemical conversion of NAD into a highly fluorescent derivative. NAD conversion is achieved by reaction acetophenone in base (KOH), followed by treatment with acid (formic acid). A simple kit may include NAD solution, 88% formic acid, 2M KOH, 20% acetophenone

(in EtoH) solution, a suitable enzyme assay buffer, and suitable control reagents. The assay may also detect genetic deficiencies involving NAD-utilizing enzymes, such as long-chain 3-hydroxyacyl-CoA dehydrogenase.

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:109240 CAPLUS

DOCUMENT NUMBER: 140:334458

TITLE: An enzymatic assay for poly(ADP-ribose) polymerase-1 (PARP-1) via the chemical quantitation of NAD+: application to the high-throughput screening of small molecules as potential inhibitors

AUTHOR(S): Putt, Karson S.; Hergenrother, Paul J.

CORPORATE SOURCE: Department of Biochemistry, University of Illinois, Urbana, IL, 61801, USA

SOURCE: Analytical Biochemistry (2004), 326(1), 78-86

CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The enzyme poly(ADP-ribose) polymerase (PARP-1) catalyzes the formation of (ADP)-ribose polymers on a variety of protein acceptors in a NAD +-dependent manner. While PARP-1 is activated by DNA damage and plays a critical role in cellular survival mechanisms, its overactivation leads to a depletion of NAD+/ATP energy stores and ultimately to necrotic cell death. Due to this dual role of PARP in the cell, small-mol. inhibitors of the PARP family of enzymes have been widely investigated for use as potentiators of anticancer therapies and as inhibitors of neurodegeneration and ischemic injuries. Unfortunately, standard assays for PARP inhibition are not optimal for the high-throughput screening of compound collections or combinatorial libraries. Described herein is a highly sensitive, inexpensive, and operationally simple assay for the rapid assessment of PARP activity that relies on the conversion of NAD+ into a highly fluorescent compound. We demonstrate that this assay can readily detect PARP inhibitors in a high-throughput screen using 384-well plates. In addition, the assay can be used to determine IC50 values

for

PARP inhibitors that have a range of inhibitory properties. As existing PARP assays utilize specialized reagents such as radiolabeled/biotinylated NAD+ or antibodies to poly(ADP-ribose), the chemical quantitation method described herein offers a highly sensitive and convenient alternative for rapidly screening compound collections for PARP inhibition.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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E2	6	NAPPEN BERNARD H/AU
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E8	1	NAPPER ANDREW DAVID/AU
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E10	1	NAPPER ANDREW MICHAEL/AU
E11	2	NAPPER ANN C/AU
E12	4	NAPPER CATHERINE E/AU


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=> e e3-e10
'E3-E10' IS NOT VALID HERE
Only one term can be used with the EXPAND command at any one time.
Enter "EXPAND" and the single E# you wish to use at the next arrow
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E4      4      MCDONAGH T A/AU
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E7     23      MCDONAGH THOMAS/AU
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4 "MCDONAGH T A"/AU
 23 "MCDONAGH THOMAS"/AU
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 OR "MCDONAGH THOMAS E"/AU OR "MCDONAGH TOM"/AU)

=> 15 or 16 or 17
 L8 122 L5 OR L6 OR L7

=> 18 and nicotinamide
 23403 NICOTINAMIDE
 431 NICOTINAMIDES
 23520 NICOTINAMIDE
 (NICOTINAMIDE OR NICOTINAMIDES)

L9 4 L8 AND NICOTINAMIDE

=> d 19 1-4 ibib abs

L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:1358125 CAPLUS
 DOCUMENT NUMBER: 146:95604
 TITLE: A microplate filtration assay using boronate-based
 affinity resin for detection of nicotinamide
 and nicotinamide-releasing enzyme, and
 screening applications
 INVENTOR(S): Curtis, Rory A.; Napper, Andrew; Hixon,
Jeffrey; Mcdonagh, Thomas
 PATENT ASSIGNEE(S): Elixir Pharmaceuticals, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 57pp., Cont.-in-part of Appl.
 No. PCT/US2004/001239.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060292652	A1	20061228	US 2005-181453	20050713
WO 2004064739	A2	20040805	WO 2004-US1239	20040116
WO 2004064739	A3	20050421		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
 PRIORITY APPLN. INFO.: US 2003-440723P P 20030116
 WO 2004-US1239 A2 20040116
 US 2004-588900P P 20040716
 US 2005-668212P P 20050404

AB Methods and compns. for evaluating nicotinamide-releasing
 activities as well as cell and organism-based evaluation methods are
 provided herein. The invention is based on novel evaluation techniques
 that can be used to evaluate nicotinamide and other related
 compds. The assays can be used to detect release of nicotinamide
 , e.g., by an enzyme. The assays are useful for evaluating enzymes
 directly or indirectly, e.g., by detecting the release of
nicotinamide. For example, the activity of NAD-dependent enzymes
 can be evaluated with these assays. The assays described here include,
 for example, assays in which a sample is contacted to a matrix that

selectively binds a precursor of nicotinamide (e.g., NAD), and that does not bind nicotinamide, such that nicotinamide generated in a sample (e.g., by an enzymic reaction) can be separated from the matrix. Exemplary boronate resin in a Multiscreen filter plate is provided which retains NAD but not nicotinamide. A microplate filtration assay was used to assay the SIRT class of enzymes and determine kinetic parameters. A method to identify human SIRT1 modulators using MEF cells is disclosed.

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1189331 CAPLUS
DOCUMENT NUMBER: 144:45011
TITLE: Discovery of Indoles as Potent and Selective Inhibitors of the Deacetylase SIRT1
AUTHOR(S): Napper, Andrew D.; Hixon, Jeffrey; McDonagh, Thomas; Keavey, Kenneth; Pons, Jean-Francois; Barker, Jonathan; Yau, Wei Tsung; Amouzegh, Patricia; Flegg, Adam; Hamelin, Estelle; Thomas, Russell J.; Kates, Michael; Jones, Stephen; Navia, Manuel A.; Saunders, Jeffrey O.; DiStefano, Peter S.; Curtis, Rory
CORPORATE SOURCE: Elixir Pharmaceuticals, Cambridge, MA, 02139, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(25), 8045-8054
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:45011

AB High-throughput screening against the human sirtuin SIRT1 led to the discovery of a series of indoles as potent inhibitors that are selective for SIRT1 over other deacetylases and NAD-processing enzymes. The most potent compds. described herein inhibit SIRT1 with IC50 values of 60-100 nM, representing a 500-fold improvement over previously reported SIRT inhibitors. Preparation of enantiomerically pure indole derivs. allowed for their characterization in vitro and in vivo. Kinetic analyses suggest that these inhibitors bind after the release of nicotinamide from the enzyme and prevent the release of deacetylated peptide and O-acetyl-ADP-ribose, the products of enzyme-catalyzed deacetylation. These SIRT1 inhibitors are low mol. weight, cell-permeable, orally bioavailable, and metabolically stable. These compds. provide chemical tools to study the biol. of SIRT1 and to explore therapeutic uses for SIRT1 inhibitors.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:862212 CAPLUS
DOCUMENT NUMBER: 144:2645
TITLE: Microplate filtration assay for nicotinamide release from NAD using a boronic acid resin
AUTHOR(S): McDonagh, Thomas; Hixon, Jeffrey; DiStefano, Peter S.; Curtis, Rory; Napper, Andrew D.
CORPORATE SOURCE: Elixir Pharmaceuticals, Cambridge, MA, 02139, USA
SOURCE: Methods (San Diego, CA, United States) (2005), 36(4), 346-350
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A microplate-based assay for NAD-dependent Class III histone deacetylases (also known as SIRT6s) that measures the enzyme-catalyzed release of nicotinamide from radiolabeled NAD, using a boronic acid resin to selectively capture the NAD. This method avoids the need for fluorogenic or radiolabeled peptides or separation of the reaction products using solvent extraction. The protocol reported here is rapid and uses com. available materials. The use of a simple microplate filtration device allows for the simultaneous processing of 96 samples, facilitating enzyme kinetic analyses and inhibition studies. Furthermore, monitoring nicotinamide release rather than peptide deacetylation obviates the need for chemical modification of protein and peptide substrates. This assay is applicable to SIRT6s and other enzymes that cleave nicotinamide from NAD.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:633449 CAPLUS

DOCUMENT NUMBER: 141:169968

TITLE: Nicotinamide assay and use for nicotinamide-releasing enzyme detection

INVENTOR(S): Napper, Andrew; Hixon, Jeffrey; Mcdonagh, Tom

PATENT ASSIGNEE(S): Elixir Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004064739	A2	20040805	WO 2004-US1239	20040116
WO 2004064739	A3	20050421		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI			
AU 2004206887	A1	20040805	AU 2004-206887	20040116
CA 2513184	A1	20040805	CA 2004-2513184	20040116
EP 1587951	A2	20051026	EP 2004-703016	20040116
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 20060292652	A1	20061228	US 2005-181453	20050713
PRIORITY APPLN. INFO.:			US 2003-440723P	P 20030116
			WO 2004-US1239	W 20040116
			US 2004-588900P	P 20040716
			US 2005-668212P	P 20050404

AB Methods and compns. for evaluating nicotinamide-releasing activities are provided herein. The invention is based, inter alia, on novel evaluation techniques that can be used to evaluate nicotinamide and other related compds. In some implementations, the assays can be used to detect release of nicotinamide, e.g., by an enzyme. The assays are useful for evaluating enzymes directly or indirectly, e.g., by detecting the release of nicotinamide. For example, the activity of NAD-dependent enzymes can be evaluated with these assays. Exemplary NAD-dependent enzymes include NAD-hydrolases, deacetylases, DNA ligases, aldehyde dehydrogenases, and toxins associated

with cholera, diphtheria, pertussis. The assays described here include, for example, assays in which a sample is contacted to a matrix that selectively binds a precursor of nicotinamide (e.g., NAD), and that does not bind nicotinamide, such that nicotinamide generated in a sample (e.g., by an enzymic reaction) can be separated from the matrix. Other exemplary assays detect nicotinamide after treatment with a nicotinamide-modifying enzyme. Enzymes such as nicotinamide deamidase and nicotinamide N-Me transferase react with nicotinamide and produce detectable compds., or precursors of detectable compds. One method, Filtration Assay of 14C-nicotinamide Release, is based on the use of boronate-based affinity resin that selectively binds 1,2-diols. 14C-labeled NAD and acetylated substrate are incubated with SIRT enzyme. Following the enzymic reaction, the release of 14C-nicotinamide from NAD may be quantified by filtration of the reaction mixture through boronate resin. The resin selectively binds excess unreacted NAD while allowing nicotinamide to flow through unbound (FIG. 2). Another method, Coupled Enzymic Assay of Nicotinamide Release (ammonia detection), is based on enzymic release of ammonia from nicotinamide and subsequent fluorometric ammonia detection. The nicotinamide released in the SIRT reaction is then converted to nicotinic acid and ammonia by addition of the enzyme nicotinamide deamidase. Ammonia is then detected by fluorometric assay using o-phthaldialdehyde (OPA) (FIG. 6). Coupled Enzymic Assay of Nicotinamide Release (N-methylnicotinamide detection) method is based on enzymic conversion of nicotinamide to N-methylnicotinamide followed by reaction of the latter with acetophenone to generate a fluorescent product. NAD and acetylated substrate (e.g., an acetylated peptide) are incubated with SIRT enzyme. The nicotinamide released in the SIRT reaction is then converted to N-methylnicotinamide by addition of the enzyme nicotinamide N-Me transferase (NNMT). Base-catalyzed reaction with acetophenone followed by acidification of the condensation product with formic acid results in ring closure to form a fluorescent product (FIG. 8). Human SIRT1 deacetylase was assayed as shown in the scheme in FIG. 2. Enzyme activity was measured by scintillation counting of the nicotinamide-containing filtrate.

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=> (detect? or assy) and fluoresc? and (nad or nadh)
    1855314 DETECT?
      42 ASSY
    521853 FLUORESC?
      42465 NAD
      229 NADS
      42670 NAD
        (NAD OR NADS)
      40788 NADH
      2 NADHS
      40788 NADH
        (NADH OR NADHS)
L10      850 (DETECT? OR ASSY) AND FLUORESC? AND (NAD OR NADH)

=> 110 and acetophenone
    42071 ACETOPHENONE
    3490 ACETOPHENONES
    43373 ACETOPHENONE
      (ACETOPHENONE OR ACETOPHENONES)
L11      5 L10 AND ACETOPHENONE
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=> d 111 1-5 ibib abs

L11 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:371413 CAPLUS

DOCUMENT NUMBER: 142:406532

TITLE: Fluorescent derivative of NAD in
methods of detecting poly(ADP-ribose)
polymerase and other NAD-utilizing enzymes

INVENTOR(S): Hergenrother, Paul J.; Putt, Karson S.

PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois,
USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005038043	A2	20050428	WO 2004-US34010	20041014
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WO 2005038043	A3	20050707		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

US 20070078100	A1	20070405	US 2006-595360	20061221
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PRIORITY APPLN. INFO.: US 2003-510916P P 20031014

WO 2004-US34010 W 20041014

AB The present invention makes use of the discovery that poly(ADP-ribose) polymerase (PARP) and other NAD-utilizing enzymes can be readily detected using a highly sensitive, convenient, simple assay that relies upon the chemical conversion of NAD into a highly fluorescent derivative NAD conversion is achieved by reaction acetophenone in base (KOH), followed by treatment with acid (formic acid). A simple kit may include NAD solution, 88% formic acid, 2M KOH, 20% acetophenone (in EtoH) solution, a suitable enzyme assay buffer, and suitable control reagents. The assay may also detect genetic deficiencies involving NAD -utilizing enzymes, such as long-chain 3-hydroxyacyl-CoA dehydrogenase.

L11 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:633449 CAPLUS

DOCUMENT NUMBER: 141:169968

TITLE: Nicotinamide assay and use for nicotinamide-releasing
enzyme detection

INVENTOR(S): Napper, Andrew; Hixon, Jeffrey; Mcdonagh, Tom

PATENT ASSIGNEE(S): Elixir Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064739	A2	20040805	WO 2004-US1239	20040116
WO 2004064739	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
AU 2004206887	A1	20040805	AU 2004-206887	20040116
CA 2513184	A1	20040805	CA 2004-2513184	20040116
EP 1587951	A2	20051026	EP 2004-703016	20040116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060292652	A1	20061228	US 2005-181453	20050713
PRIORITY APPLN. INFO.:			US 2003-440723P	P 20030116
			WO 2004-US1239	W 20040116
			US 2004-588900P	P 20040716
			US 2005-668212P	P 20050404

AB Methods and compns. for evaluating nicotinamide-releasing activities are provided herein. The invention is based, inter alia, on novel evaluation techniques that can be used to evaluate nicotinamide and other related compds. In some implementations, the assays can be used to detect release of nicotinamide, e.g., by an enzyme. The assays are useful for evaluating enzymes directly or indirectly, e.g., by detecting the release of nicotinamide. For example, the activity of NAD-dependent enzymes can be evaluated with these assays. Exemplary NAD-dependent enzymes include NAD-hydrolases, deacetylases, DNA ligases, aldehyde dehydrogenases, and toxins associated with cholera, diphtheria, pertussis. The assays described here include, for example, assays in which a sample is contacted to a matrix that selectively binds a precursor of nicotinamide (e.g., NAD), and that does not bind nicotinamide, such that nicotinamide generated in a sample (e.g., by an enzymic reaction) can be separated from the matrix. Other exemplary assays detect nicotinamide after treatment with a nicotinamide-modifying enzyme. Enzymes such as nicotinamide deamidase and nicotinamide N-Me transferase react with nicotinamide and produce detectable compds., or precursors of detectable compds. One method, Filtration Assay of ¹⁴C-nicotinamide Release, is based on the use of boronate-based affinity resin that selectively binds 1,2-diols. ¹⁴C-labeled NAD and acetylated substrate are incubated with SIRT enzyme. Following the enzymic reaction, the release of ¹⁴C-nicotinamide from NAD may be quantified by filtration of the reaction mixture through boronate resin. The resin selectively binds excess unreacted NAD while allowing nicotinamide to flow through unbound (FIG. 2). Another method, Coupled Enzymic Assay of Nicotinamide Release (ammonia detection), is based on enzymic release of ammonia from nicotinamide and subsequent fluorometric ammonia detection. The nicotinamide released in the SIRT reaction is then converted to nicotinic acid and ammonia by addition of the enzyme nicotinamide deamidase. Ammonia is then detected by fluorometric assay using o-phthaldialdehyde (OPA) (FIG. 6). Coupled Enzymic Assay of Nicotinamide Release (N-methylnicotinamide detection) method is based on enzymic conversion of nicotinamide to N-methylnicotinamide followed by reaction of the latter with acetophenone to generate a fluorescent product. NAD and acetylated substrate (e.g., an acetylated peptide) are incubated with SIRT enzyme. The nicotinamide released in the SIRT reaction is then converted to N-methylnicotinamide by addition of the enzyme nicotinamide N-Me transferase (NNMT). Base-catalyzed reaction with

acetophenone followed by acidification of the condensation product with formic acid results in ring closure to form a fluorescent product (FIG. 8). Human SIRT1 deacetylase was assayed as shown in the scheme in FIG. 2. Enzyme activity was measured by scintillation counting of the nicotinamide-containing filtrate.

L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:109240 CAPLUS

DOCUMENT NUMBER: 140:334458

TITLE: An enzymatic assay for poly(ADP-ribose) polymerase-1 (PARP-1) via the chemical quantitation of NAD +: application to the high-throughput screening of small molecules as potential inhibitors

AUTHOR(S): Putt, Karson S.; Hergenrother, Paul J.

CORPORATE SOURCE: Department of Biochemistry, University of Illinois, Urbana, IL, 61801, USA

SOURCE: Analytical Biochemistry (2004), 326(1), 78-86

CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The enzyme poly(ADP-ribose) polymerase (PARP-1) catalyzes the formation of (ADP)-ribose polymers on a variety of protein acceptors in a NAD +-dependent manner. While PARP-1 is activated by DNA damage and plays a critical role in cellular survival mechanisms, its overactivation leads to a depletion of NAD+/ATP energy stores and ultimately to necrotic cell death. Due to this dual role of PARP in the cell, small-mol. inhibitors of the PARP family of enzymes have been widely investigated for use as potentiators of anticancer therapies and as inhibitors of neurodegeneration and ischemic injuries. Unfortunately, standard assays for PARP inhibition are not optimal for the high-throughput screening of compound collections or combinatorial libraries. Described herein is a highly sensitive, inexpensive, and operationally simple assay for the rapid assessment of PARP activity that relies on the conversion of NAD + into a highly fluorescent compound We demonstrate that this assay can readily detect PARP inhibitors in a high-throughput screen using 384-well plates. In addition, the assay can be used to determine IC50 values for PARP inhibitors that have a range of inhibitory properties. As existing PARP assays utilize specialized reagents such as radiolabeled/biotinylated NAD + or antibodies to poly(ADP-ribose), the chemical quantitation method described herein offers a highly sensitive and convenient alternative for rapidly screening compound collections for PARP inhibition.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:109239 CAPLUS

DOCUMENT NUMBER: 141:19451

TITLE: Application of the measurement of oxidized pyridine dinucleotides with high-performance liquid chromatography-fluorescence detection to assay the uncoupled oxidation of NADPH by neuronal nitric oxide synthase

AUTHOR(S): Palfi, Melinda; Halasz, Attila Sandor; Tabi, Tamas; Magyar, Kalman; Szoko, Eva

CORPORATE SOURCE: Department of Pharmacodynamics, Semmelweis University, Budapest, H-1089, Hung.

SOURCE: Analytical Biochemistry (2004), 326(1), 69-77

CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and sensitive high-performance liquid chromatog. method has been developed for the measurement of oxidized pyridine dinucleotides (NAD⁺, NADP⁺) in biol. samples following fluorescence derivatization. Under strongly alkaline conditions the pyridinium ring of the nicotinamide moiety reacts with carbonyl compds., resulting in stable fluorescent products. Upon subsequent addition of concentrated formic acid and treatment with heat, this fluorescence is further amplified and is shifted to higher-wavelength regions. From among the ketones assayed (acetone, ethylmethyl ketone, acetophenone) the condensation product with acetophenone possesses the highest molar relative fluorescence, thus allowing the most sensitive detection in our exptl. setup (limit of detection: 0.02 pmol/50 μ l injected volume). The fluorescent products have been separated on a reverse-phase C-18 column using 0.1 M citric acid (pH 3.2)/acetonitrile (92/8, volume/volume) as mobile phase. Our method is suitable for assaying NADH- and NADPH-dependent enzyme reactions by quantifying oxidized coenzyme products. As an example, the activity of neuronal nitric oxide synthase (nNOS), a NADPH-requiring enzyme, has been assessed by measuring the products NADP⁺ and L-citrulline at various substrate (L-arginine) concns. The rate of the uncoupled NADPH oxidation by nNOS can be estimated from the ratio of NADP⁺/L-citrulline produced.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:419251 CAPLUS

DOCUMENT NUMBER: 103:19251

ORIGINAL REFERENCE NO.: 103:3147a,3150a

TITLE: High-performance liquid chromatographic determination of N1-alkylnicotinamide in urine

AUTHOR(S): Hirayama, Teruhisa; Yoshida, Koichi; Uda, Kazuhiko; Nohara, Motoshi; Fukui, Shozo

CORPORATE SOURCE: Kyoto Pharm. Univ., Kyoto, 607, Japan

SOURCE: Analytical Biochemistry (1985), 147(1), 108-13
CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A simple HPLC method was developed for determining N1-alkylnicotinamides, including C1-C5 alkyl derivs., in urine. N1-Alkylnicotinamides were treated with acetophenone in strong alkali medium at 0° and then formic acid was added. The reaction mixture was heated in acidic medium at above 93°, and the fluorescent product, 1-alkyl-7-phenyl-1,5-dihydro-5-oxo-1,6-naphthyridine, was chromatographed by HPLC, using a Zorbax SCX-300 column with a mixed mobile phase of MeCN-0.04M NH₄ phosphate, monobasic. N1-Alkylnicotinamides can be determined as 1,6-naphthyridine derivs. by a fluorometric detector at a level of 100 pg (signal/noise = 2). Recoveries of N1-alkylnicotinamides in urine were satisfactory. Interfering reaction products from NAD⁺ and NADP⁺ were clearly eliminated for determination of N1-alkylnicotinamides without pentyl derivs.

=> 110 and parp

4624 PARP

89 PARPS

4634 PARP

(PARP OR PARPS)

L12

4 L10 AND PARP

=> d l12 1-4 ibib abs

L12 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:371413 CAPLUS

DOCUMENT NUMBER: 142:406532

TITLE: Fluorescent derivative of NAD in
methods of detecting poly(ADP-ribose)
polymerase and other NAD-utilizing enzymes

INVENTOR(S): Hergenrother, Paul J.; Putt, Karson S.

PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois,
USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005038043	A2	20050428	WO 2004-US34010	20041014
WO 2005038043	A3	20050707		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20070078100	A1	20070405	US 2006-595360	20061221
PRIORITY APPLN. INFO.:			US 2003-510916P	P 20031014
			WO 2004-US34010	W 20041014

AB The present invention makes use of the discovery that poly(ADP-ribose) polymerase (PARP) and other NAD-utilizing enzymes can be readily detected using a highly sensitive, convenient, simple assay that relies upon the chemical conversion of NAD into a highly fluorescent derivative NAD conversion is achieved by reaction acetophenone in base (KOH), followed by treatment with acid (formic acid). A simple kit may include NAD solution, 88% formic acid, 2M KOH, 20% acetophenone (in EtOH) solution, a suitable enzyme assay buffer, and suitable control reagents. The assay may also detect genetic deficiencies involving NAD-utilizing enzymes, such as long-chain 3-hydroxyacyl-CoA dehydrogenase.

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:109240 CAPLUS

DOCUMENT NUMBER: 140:334458

TITLE: An enzymatic assay for poly(ADP-ribose) polymerase-1 (PARP-1) via the chemical quantitation of NAD+: application to the high-throughput screening of small molecules as potential inhibitors

AUTHOR(S): Putt, Karson S.; Hergenrother, Paul J.

CORPORATE SOURCE: Department of Biochemistry, University of Illinois,
Urbana, IL, 61801, USA
SOURCE: Analytical Biochemistry (2004), 326(1), 78-86
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The enzyme poly(ADP-ribose) polymerase (PARP-1) catalyzes the formation of (ADP)-ribose polymers on a variety of protein acceptors in a NAD⁺-dependent manner. While PARP-1 is activated by DNA damage and plays a critical role in cellular survival mechanisms, its overactivation leads to a depletion of NAD⁺/ATP energy stores and ultimately to necrotic cell death. Due to this dual role of PARP in the cell, small-mol. inhibitors of the PARP family of enzymes have been widely investigated for use as potentiators of anticancer therapies and as inhibitors of neurodegeneration and ischemic injuries. Unfortunately, standard assays for PARP inhibition are not optimal for the high-throughput screening of compound collections or combinatorial libraries. Described herein is a highly sensitive, inexpensive, and operationally simple assay for the rapid assessment of PARP activity that relies on the conversion of NAD⁺ into a highly fluorescent compound. We demonstrate that this assay can readily detect PARP inhibitors in a high-throughput screen using 384-well plates. In addition, the assay can be used to determine IC₅₀ values for PARP inhibitors that have a range of inhibitory properties. As existing PARP assays utilize specialized reagents such as radiolabeled/biotinylated NAD⁺ or antibodies to poly(ADP-ribose), the chemical quantitation method described herein offers a highly sensitive and convenient alternative for rapidly screening compound collections for PARP inhibition.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:700031 CAPLUS
DOCUMENT NUMBER: 130:63173
TITLE: In situ staining for poly(ADP-ribose) polymerase activity using an NAD analog
AUTHOR(S): Davis, R. Eric; Mysore, Veena; Browning, Jared C.; Hsieh, Joseph C.; Lu, Quynh-Anh T.; Katsikis, Peter D.
CORPORATE SOURCE: Department of Pathology, Stanford University Medical Center, Palo Alto, CA, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1998), 46(11), 1279-1289
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Poly(ADP-ribose) polymerase (PARP) is a highly abundant nuclear enzyme which metabolizes NAD, in response to DNA strand breakage, to produce chains of poly(ADP-ribose) attached to nuclear proteins. PARP activation has been implicated in ischemia/reperfusion injury, but its biol. significance is not fully understood. We have modified an existing in situ method for detection of PARP activity by using an NAD analog in which adenine is modified by an "etheno" (vinyl) bridge. Etheno-NAD serves as a PARP substrate in an initial enzymic reaction; a specific antibody to ethenoadenosine is then used in an immunohistochem. reaction to detect the production of modified poly(ADP-ribose). The method produces strong and specific labeling of

nuclei in which PARP has been activated, i.e., those in which DNA strand breaks have been produced, and the results can be analyzed by microscopy, flow cytometry, or colorimetry. The method is applicable to cultured cells in several formats and to frozen tissue sections. The particular characteristics of the new method may assist in future in situ studies of PARP activation.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:293104 CAPLUS

DOCUMENT NUMBER: 127:3458

ORIGINAL REFERENCE NO.: 127:799a,802a

TITLE: Intact cell evidence for the early synthesis, and subsequent late apopain-mediated suppression, of poly(ADP-ribose) during apoptosis

AUTHOR(S): Rosenthal, Dean S.; Ding, Ruchuang; Simbulan-Rosenthal, Cynthia M. G.; Vaillancourt, John P.; Nicholson, Donald W.; Smulson, Mark

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University School of Medicine, Washington, DC, 20007, USA

SOURCE: Experimental Cell Research (1997), 232(2), 313-321
CODEN: ECREAL; ISSN: 0014-4827

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Poly(ADP-ribose) polymerase (PARP), which is catalytically activated by DNA strand breaks, has been implicated in apoptosis, or programmed cell death. A protease (CPP32) responsible for the cleavage of PARP and necessary for apoptosis was recently purified and characterized. The coordinated sequence of events related to PARP activation and cleavage in apoptosis has now been examined in individual cells. Apoptosis was studied in a human osteosarcoma cell line that undergoes a slow (8 to 10 days), spontaneous, and reproducible death program in culture. Changes in the abundance of intact PARP, poly(ADP-ribose) (PAR), and a proteolytic cleavage product of PARP that contains the DNA-binding domain were examined during apoptosis in the context of individual, whole cells by immunofluorescence with specific antibodies. The synthesis of PAR from NAD increased early, within 2 days of cell plating for apoptosis, prior to the appearance of internucleosomal DNA cleavage and before the cells become irreversibly committed to apoptosis, since replating yields viable, nonapoptotic cells. Strong expression of full-length PARP was also detected, by immunofluorescence as well as by Western anal., during this same time period. However, after .apprx.4 days in culture, the abundance of both full-length PARP and PAR decreased markedly. After 6 days, a proteolytic cleavage product containing the DNA-binding domain of PARP was detected immunocytochem. and confirmed by Western anal., both in the nuclei and in the cytoplasm of cells. A recombinant peptide spanning the DNA-binding domain of PARP was expressed, purified, and biotinylated, and was then used as a probe for DNA strand breaks. Fluorescence microscopy with this probe revealed extensive DNA fragmentation during the later stages of apoptosis. This is the first report, using individual, intact cells, demonstrating that poly(ADP-ribosyl)ation of nuclear proteins occurs prior to the commitment to apoptosis, that inactivation and cleavage of PARP begin shortly thereafter, and that very little PAR per se is present during the later stages of apoptosis, despite the presence of a very large number of DNA strand breaks. These results suggest a neg. regulatory role for

PARP during apoptosis, which in turn may reflect the requirement for adequate NAD and ATP during the later stages of programmed cell death.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> l13 not l11 not l12

L14 5 L13 NOT L11 NOT L12

=> d l14 1-5 ibib abs

L14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1017520 CAPLUS

DOCUMENT NUMBER: 143:381768

TITLE: Bacterial cyanide oxygenase is a suite of enzymes catalyzing the scavenging and adventitious utilization of cyanide as a nitrogenous growth substrate

AUTHOR(S): Fernandez, Ruby F.; Kunz, Daniel A.

CORPORATE SOURCE: Division of Biochemistry and Molecular Biology, Department of Biological Sciences, University of North Texas, Denton, TX, 76203-5220, USA

SOURCE: Journal of Bacteriology (2005), 187(18), 6396-6402

CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cyanide oxygenase (CNO) from *Pseudomonas fluorescens* NCIMB 11764 catalyzes the pterin-dependent oxygenolytic cleavage of cyanide (CN) to formic acid and ammonia. CNO was resolved into four protein components (P1 to P4), each of which along with a source of pterin cofactor was obligately required for CNO activity. Component P1 was characterized as a multimeric 230-kDa flavoprotein exhibiting the properties of a peroxide-forming NADH oxidase (oxidoreductase) (Nox). P2 consisted of a 49.7-kDa homodimer that showed 100% amino acid identity at its N terminus to NADH peroxidase (Npx) from *Enterococcus faecalis*. Enzyme assays further confirmed the identities of both Nox and Npx enzymes (specific activity, 1 U/mg). P3 was characterized as a large oligomeric protein (.apprx.300 kDa) that exhibited cyanide dihydratase (CynD) activity (specific activity, 100 U/mg). Two polypeptides of 38 kDa and 43 kDa were each detected in the isolated enzyme, the former believed to confer catalytic activity based on its similar size to other CynD enzymes. The amino acid sequence of an internal peptide of the 43-kDa protein was 100% identical to bacterial elongation factor Tu, suggesting a role as a possible chaperone in the assembly of CynD or a multienzyme CNO complex. The remaining P4 component consisted of a 28.9-kDa homodimer and was identified as carbonic anhydrase (specific activity, 2000 U/mg). While the function of participating pterin and the roles of Nox, Npx, CynD, and CA in the CNO-catalyzed scavenging of CN remain to be determined, this is the first report describing the collective involvement of these four enzymes in the metabolic detoxification and utilization of CN as a bacterial nitrogenous growth substrate.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:83802 CAPLUS

DOCUMENT NUMBER: 139:257560

TITLE: Picomolar analysis of flavins in biological samples by

dynamic pH junction-sweeping capillary electrophoresis with laser-induced fluorescence detection

AUTHOR(S): Britz-McKibbin, Philip; Markuszewski, Michal J.; Iyanagi, Takashi; Matsuda, Keiko; Nishioka, Takaaki; Terabe, Shigeru

CORPORATE SOURCE: Graduate School of Science, Department of Material Sciences, Himeji Institute of Technology, Kamigori, Hyogo, 678-1297, Japan

SOURCE: Analytical Biochemistry (2003), 313(1), 89-96
CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sensitive capillary electrophoresis (CE) methods are required for emerging areas of biochem. research such as the metabolome. In this report, dynamic pH junction-sweeping CE with laser-induced fluorescence (LIF) detection is applied as a robust single method to analyze trace amts. of three flavin derivs., riboflavin, FMN, and FAD, from several types of samples including bacterial cell exts., recombinant protein, and biol. fluids. Submicromolar amts. of flavin coenzymes were measured directly from formic acid cell exts. of *Bacillus subtilis*. Significant differences in flavin concentration were measured in cell exts. derived from either glucose or malate as the carbon source in the culture media. Quant. assessment of FAD and FMN content from selected flavoenzymes was demonstrated after heat denaturation to release noncovalently bound coenzymes and deproteinization. This method was also applied to the anal. of free flavins in pooled human plasma and urine without the need for laborious off-line sample preconcn. Picomolar detectability of flavins by CE-LIF detection was realized with online preconcn. (up to 15% capillary length used for injection) by dynamic pH junction-sweeping, resulting in a limit of detection (S/N=3) of about 4.0 pM for FAD and FMN. This represents over a 60-fold improvement in concentration sensitivity compared to those of previous techniques using conventional injections. The method was validated in terms of reproducibility, sensitivity, linearity, and specificity. Flavin anal. by dynamic pH junction-sweeping CE-LIF offers a simple, yet sensitive way to analyze trace levels of flavin metabolites from complex biol. samples.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:99367 CAPLUS

TITLE: A habitat for psychrophiles in deep Antarctic ice

AUTHOR(S): Price, P. Buford

CORPORATE SOURCE: Physics Department, University of California, Berkeley, CA, 94720, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(3), 1247-1251
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microbes, some of which may be viable, have been found in ice cores drilled at Vostok Station at depths down to $\approx 3,600$ m, close to the surface of the huge subglacial Lake Vostok. Two types of ice have been found. The upper 3,500 m comprises glacial ice containing traces of nutrients of aeolian origin including sulfuric acid, nitric acid, methanosulfonic

acid (MSA), formic acid, sea salts, and mineral grains. Ice below $\approx 3,500$ m comprises refrozen water from Lake Vostok, accreted to the bottom of the glacial ice. Nutrients in the accretion ice include salts and dissolved organic carbon. There is great interest in searching for living microbes and especially for new species in deepest Antarctic ice. I propose a habitat consisting of interconnected liquid veins along three-grain boundaries in ice in which psychrophilic bacteria can move and obtain energy and carbon from ions in solution. In the accretion ice, with an age of a few 10⁴ years and a temperature a few degrees below freezing, the carbon and energy sources in the veins can maintain significant nos. of cells per cubic centimeter that are metabolizing but not multiplying. In the 4 + 10⁵-year-old colder glacial ice, at least 1 cell per cm³ in acid veins can be maintained. With fluorescence microscopy tuned to detect NADH in live organisms, motile bacteria could be detected by direct scanning of the veins in ice samples.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1992:253977 CAPLUS

DOCUMENT NUMBER: 116:253977

ORIGINAL REFERENCE NO.: 116:43059a, 43062a

TITLE: On-line fluorescence-monitoring of the methanogenic fermentation

AUTHOR(S): Peck, Michael W.; Chynoweth, David P.

CORPORATE SOURCE: Agric. Eng. Dep., Univ. Florida, Gainesville, FL, 32611, USA

SOURCE: Biotechnology and Bioengineering (1992), 39(11), 1151-60

CODEN: BIBIAU; ISSN: 0006-3592

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Online in situ fluorescence measurements of methanogenic fermentation were conducted with a reactor receiving either glucose or a mixture of volatile fatty acids as the substrate. The reactors were perturbed from steady-state conditions in order to assess the response of fluorescence-monitoring probes. Two fluorescence-monitoring probes were evaluated over a period of 8 mo; they performed in a consistent manner, and their response was not significantly affected by the changes in pH and redox potential encountered during routine reactor operation. A com. available probe, designed to measure NAD(P)H, demonstrated particular promise for detecting imbalance caused by the entry of air, inhibitor addition and was capable of distinguishing between different substrates. This fluorescence-monitoring probe detected imbalance more rapidly than other online measurements such as pH, Eh, or gas production, or off-line measurements such as volatile fatty acid concentration or gas composition. An exptl. fluorescence-monitoring probe, designed to measure coenzyme F420 also showed some promise in this regard. The response of the fluorescence-monitoring probes also revealed details of the metabolic routes in the reactors and the probes represent a useful research tool. For example, a failure to observe the characteristic response to the NAD(P)H-monitoring probe to formate addition during the metabolism of acetate, propionate, or glucose strongly suggests that any formate liberated during their catabolism is degraded via a different route to exogenously added formate.

L14 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1982:175414 CAPLUS

DOCUMENT NUMBER: 96:175414
ORIGINAL REFERENCE NO.: 96:28811a,28814a
TITLE: Improved estimation of formate in body fluids and tissues
AUTHOR(S): Makar, A. B.; Tephly, T. R.
CORPORATE SOURCE: Toxicol. Cent., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Clinical Chemistry (Washington, DC, United States) (1982), 28(2), 385
CODEN: CLCHAU; ISSN: 0009-9147
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An improved method for detecting formic acid [64-18-6] concns. ≥ 0.2 mg/L in body fluids and tissues is described. The key substance used in the assay is formate dehydrogenase (EC 1.2.1.2) [9028-85-7] and the anal. is done in 2 steps. In the 1st step, a 0.1-mL sample of blood, urine, or tissue extract is mixed with 0.1 of 10 mmol/L NAD⁺ solution, 0.1 mL of K phosphate buffer (pH 7.4, 20 mmol/L), and 50 μ L of formate dehydrogenase solution. The mixture is incubated for 15 min at 37°, then 0.1 mL of diaphorase solution (4 U/mL), 50 μ L of resazurin solution (0.2 mg/mL), and 0.5 mL of phosphate buffer (pH 6.00, 200 mmol/L) are added. The contents of the tubes are mixed and the incubation continued for 5 more minutes at 37°. The reaction tubes are then immersed in boiling water for 3 min and cooled to room temperature. Then, 5.0 mL of distilled water is added to each tube, the contents are mixed, and the fluorescence is measured in an Minco-Bowman spectrophotofluorometer. An excitation wavelength of 565 nm and an emission wavelength of 590 nm are used. A standard curve is prepared with use of 0.2-2.5 μ g of formate/mL each time that an anal. is performed. Important advantages of this system over systems previously described are discussed.

=> l16 not (l11 or l12 or l13)

L17 5 L16 NOT (L11 OR L12 OR L13)

=> d l17 1-5 ibib abs

L17 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:11559 CAPLUS
DOCUMENT NUMBER: 148:278677
TITLE: Kinetic studies of Escherichia coli AlkB using a new fluorescence-based assay for DNA demethylation
AUTHOR(S): Roy, Todd W.; Bhagwat, A. S.
CORPORATE SOURCE: Department of Chemistry, Wayne State University, Detroit, MI, 48202, USA
SOURCE: Nucleic Acids Research (2007), 35(21), e147/1-e147/7
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Escherichia coli AlkB protein catalyzes the direct reversal of alkylation damage to DNA; primarily 1-methyladenine (1 mA) and 3-methylcytosine (3 mC) lesions created by endogenous or environmental alkylating agents. AlkB is a member of the non-heme iron (II) α -ketoglutarate-dependent dioxygenase superfamily, which removes the alkyl group through oxidation eliminating a Me group as formaldehyde. We have developed a fluorescence-based assay for the dealkylation activity of this family of enzymes. It uses formaldehyde dehydrogenase to convert formaldehyde to formic acid and monitors the creation of an NADH analog using

fluorescence. This assay is a great improvement over the existing assays for DNA demethylation in that it is continuous, rapid and does not require radioactively labeled material. It may also be used to study other demethylation reactions including demethylation of histones. We used it to determine the kinetic consts. for AlkB and found them to be somewhat different than previously reported values. The results show that AlkB demethylates 1 mA and 3 mC with comparable efficiencies and has only a modest preference for a single-stranded DNA substrate over its double-stranded DNA counterpart.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1234964 CAPLUS
DOCUMENT NUMBER: 148:92157
TITLE: HTS model for poly (ADP-ribose) polymerase-1 inhibitors
AUTHOR(S): Liu, Jun; Zhang, Luyong
CORPORATE SOURCE: Center of New Drug Screening, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Tongbao (2007), 23(1), 124-127
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The aim of this paper is to introduce a high throughput screen model for PARP-1 inhibitors. Setting up an assay for PARP-1 activity relies on the conversion of NAD⁺ into a highly fluorescent compound. The inhibitory effects of 9280 samples (including pure organic compds., exts. from plants and exts. from microorganism) were screened by the high throughout assay. One hundred and forty-eight compds. had inhibitory effects over 70%. Ultimately, three inhibitors were identified as PARP-1 inhibitor with high activity. The high throughput screening was a highly sensitive, inexpensive, and operationally simple assay method in identifying PARP-1 inhibitors.

L17 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:795945 CAPLUS
DOCUMENT NUMBER: 132:32676
TITLE: Isolation of poly(ADP-ribose)polymerase genes and application for diagnosis and gene therapy
INVENTOR(S): Kock, Michael; Hoyer, Thomas; Kroger, Burkhard; Otterbach, Bernd; Lubisch, Wilfried; Lemaire, Hans-Georg
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9964572	A2	19991216	WO 1999-EP3889	19990604
WO 9964572	A3	20000608		
W:	AL, AU, BG, BR, BY, CA, CN, CZ, GE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, ZA, AM, AZ, KG, MD, TJ, TM			

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE

CA 2330206	A1	19991216	CA 1999-2330206	19990604
AU 9946059	A	19991230	AU 1999-46059	19990604
BR 9910967	A	20010213	BR 1999-10967	19990604
EP 1082416	A2	20010314	EP 1999-929144	19990604
EP 1082416	B1	20070328		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
SI, FI, RO

TR 200003624	T2	20010621	TR 2000-3624	19990604
HU 2001003190	A2	20011228	HU 2001-3190	19990604
JP 2002517231	T	20020618	JP 2000-553562	19990604
AT 358175	T	20070415	AT 1999-929144	19990604
ES 2285842	T3	20071116	ES 1999-929144	19990604
MX 2000PA11567	A	20020327	MX 2000-PA11567	20001124
NO 2000006153	A	20010202	NO 2000-6153	20001204
BG 105018	A	20011231	BG 2000-105018	20001204
IN 2000CN00880	A	20050304	IN 2000-CN880	20001222
HR 2001000013	A1	20011231	HR 2001-13	20010104
ZA 2001000084	A	20020104	ZA 2001-84	20010104

PRIORITY APPLN. INFO.:

DE 1998-19825213	A	19980605
DE 1999-19908837	A	19990301
WO 1999-EP3889	W	19990604

AB The invention relates to poly(ADP-ribose)polymerase (PARP) homologs which are characterized by an amino acid sequence with (a) a functional NAD⁺-binding site and (b) no zinc-finger-sequence motif of general formula CX₂CX_mHX₂C, wherein m is an integral number 28 or 30 and the radicals X represent any amino acid, independently of each other; and to the functional equivalent of said poly(ADP-ribose)polymerase (PARP) homologs. The invention also relates to nucleic acids coding the poly(ADP-ribose)polymerase (PARP) homologs, to antibodies with specificity for the novel protein, to pharmaceutical and gene therapy agents containing the inventive products, to methods for anal. determining the inventive proteins and nucleic acids, to methods for identifying the effectors or bonding partners of the inventive proteins, to novel PARP effectors and to methods for determining the effectiveness of effectors of this type.

L17 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:209647 CAPLUS

DOCUMENT NUMBER: 131:54914

TITLE: Activation of Poly [ADP-Ribose] Polymerase in Endothelial Cells and Keratinocytes: Role in an in Vitro Model of Sulfur Mustard-Mediated Vesication

AUTHOR(S): Hinshaw, Daniel B.; Lodhi, Irfan J.; Hurley, Lauren L.; Atkins, Kevin B.; Dabrowska, Milena I.

CORPORATE SOURCE: Department of Surgery, Department of Veterans Affairs Medical Center, Ann Arbor, MI, USA

SOURCE: Toxicology and Applied Pharmacology (1999), 156(1), 17-29

CODEN: TXAPA9; ISSN: 0041-008X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although endothelial cells and keratinocytes appear to be the primary cellular targets of sulfur mustard (SM), the role of the nuclear enzyme poly (ADP-ribose) polymerase (PARP) in SM-induced vesication has not been clearly defined. PARP is thought to play a crucial role in DNA repair mechanisms following exposure to alkylating agents like

SM. Using a combination of fluorescence microscopy and biochem. assays, we tested the hypothesis that SM causes activation of PARP in endothelial cells and keratinocytes with subsequent loss of NAD (NAD) and depletion of ATP levels. To determine if PARP activation accounts for SM-induced vesication, keratinocyte adherence and permeability of endothelial monolayers were measured as in vitro correlates of vesication. As early as 2 to 3 h after exposure to SM concns. as low as 250 μ M, dramatic changes were induced in keratinocyte morphol. and microfilament architecture. Exposure to 500 μ M SM induced a fourfold increase in PARP activity in endothelial cells, and a two- to threefold increase in keratinocytes. SM induced a dose-related loss of NAD⁺ in both endothelial cells and keratinocytes. ATP levels fell to .apprx.50% of control levels in response to SM concns. \geq 500 μ M. SM concns. \geq 250 μ M significantly reduced keratinocyte adherence as early as 3 h after exposure. Endothelial monolayer permeability increased substantially with concns. of SM $>$ 250 μ M. These observations support the hypothesis that the pathogenic events necessary for SM-induced vesication (i.e., capillary leak and loss of keratinocyte adherence) at higher vesicating doses of SM (\geq 500 μ M) may depend on NAD loss with PARP activation and subsequent ATP-dependent effects on microfilament architecture. Vesication developing as a result of exposure to lower concns. of SM presumably occurs by mechanisms that do not depend on loss of cellular ATP (e.g., apoptosis and direct SM-mediated damage to integrins and the basement membrane). (c) 1999 Academic Press.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:73621 CAPLUS

DOCUMENT NUMBER: 102:73621

ORIGINAL REFERENCE NO.: 102:11455a,11458a

TITLE: An enzymic method for the analysis of formate in human plasma

AUTHOR(S): Shahangian, Shahram; Ash, K. Owen; Rollins, Douglas E.

CORPORATE SOURCE: Med. Cent., Univ. Utah, Salt Lake City, UT, 84132, USA

SOURCE: Journal of Analytical Toxicology (1984), 8(6), 273-6

CODEN: JATOD3; ISSN: 0146-4760

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An enzymic method for the determination of plasma formic acid [64-18-6] concentration is described. Formate dehydrogenase is used to reduce NAD⁺ to NADH in the presence of formate. The resulting NADH then reduces the dye resazurin to resorufin, a reaction catalyzed by the endogenous diaphorase of the plasma. The generated resorufin is then measured fluorometrically by exciting it at 565 nm and quantitating the emitted light at 590 nm. The method uses the patient's plasma as the blank and as the matrix for the construction of a patient-specific formate calibration curve. The blank contains all components of the assay system except the formate dehydrogenase. Formate concentration is determined from the calibration curve, constructed by adding known quantities of Na formate to the plasma base, and plotting the fluorescence intensity against formate concentration. The assay which is sensitive to a formate level of 7 mg/L may be useful in cases where formate is a metabolite.

=> d his

(FILE 'HOME' ENTERED AT 15:49:38 ON 25 JUL 2008)

FILE 'CAPLUS' ENTERED AT 15:50:17 ON 25 JUL 2008

E HERGENROTHER/AU
E HERGENROTHER P/AU
L1 383 S E4-E10
E PUTT K/AU
L2 21 S E4-E7
L3 385 L1 OR L2
L4 7 L3 AND (NAD OR NADH)
E NAPPER A/AU
L5 51 S E3-E10
E HIXON J/AU
L6 52 S E3-E8
E MCDONAGH T/AU
L7 39 S E3 OR E4 OR E7-E9
L8 122 L5 OR L6 OR L7
L9 4 L8 AND NICOTINAMIDE
L10 850 (DETECT? OR ASSY) AND FLUORESC? AND (NAD OR NADH)
L11 5 L10 AND ACETOPHENONE

FILE 'STNGUIDE' ENTERED AT 15:55:20 ON 25 JUL 2008

FILE 'CAPLUS' ENTERED AT 15:56:02 ON 25 JUL 2008

L12 4 L10 AND PARP
L13 9 L10 AND "FORMIC ACID"
L14 5 L13 NOT L11 NOT L12
L15 1131 (DETECT? OR ASSAY) AND FLUORESC? AND (NAD OR NADH)
L16 17 L15 AND (ACETOPHENONE OR PARP OR "FORMIC ACID")
L17 5 L16 NOT (L11 OR L12 OR L13)

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NEWS	6	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
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NEWS	8	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
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NEWS	10	APR 28	IMSRESEARCH reloaded with enhancements
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NEWS	12	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	13	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	14	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	15	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	16	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS	17	JUN 25	CA/CAPplus and USPAT databases updated with IPC reclassification data
NEWS	18	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS	19	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS	20	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS	21	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS	22	JUL 28	CA/CAPplus patent coverage enhanced
NEWS	23	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS	24	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
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FILE 'HOME' ENTERED AT 17:36:14 ON 29 JUL 2008

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:36:28 ON 29 JUL 2008

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STRUCTURE FILE UPDATES: 28 JUL 2008 HIGHEST RN 1036756-19-0

DICTIONARY FILE UPDATES: 28 JUL 2008 HIGHEST RN 1036756-19-0

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

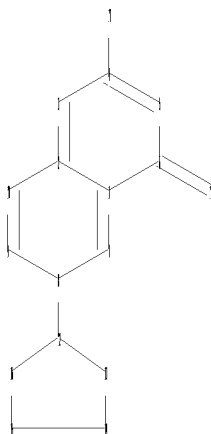
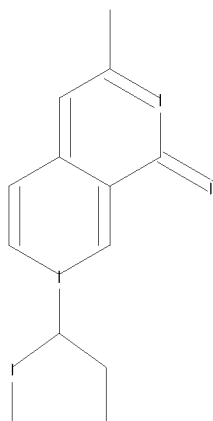
<http://www.cas.org/support/stngen/stndoc/properties.html>

=>Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=>

Uploading C:\Program Files\Stnexp\Queries\10595360\structure.str



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11
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16
ring/chain nodes :
17
chain bonds :
4-17 6-11 8-12
ring bonds :
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15-16
exact/norm bonds :
1-2 1-6 1-7 2-3 2-10 3-4 4-5 5-6 6-11 7-8 8-9 8-12 9-10 12-13 12-16
13-14 14-15 15-16
exact bonds :
4-17

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS

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L1 STRUCTURE UPLOADED

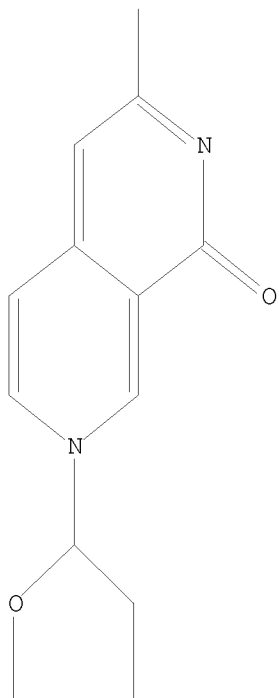
=> que L1

L2 QUE L1

=> d

L2 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

L2 QUE ABB=ON PLU=ON L1

=> s l1

SAMPLE SEARCH INITIATED 17:36:40 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 105 TO ITERATE

100.0% PROCESSED 105 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

 BATCH **COMPLETE**

PROJECTED ITERATIONS: 1486 TO 2714

PROJECTED ANSWERS: 0 TO 0

L3 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 17:36:44 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 2016 TO ITERATE

100.0% PROCESSED 2016 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

L4 5 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

178.36

178.57

FILE 'CAPLUS' ENTERED AT 17:36:48 ON 29 JUL 2008

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FILE COVERS 1907 - 29 Jul 2008 VOL 149 ISS 5
FILE LAST UPDATED: 28 Jul 2008 (20080728/ED)

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<http://www.cas.org/legal/infopolicy.html>

=> s 14

L5 4 L4

=> d 15 1-4 ibib abs hitstr

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:371413 CAPLUS

DOCUMENT NUMBER: 142:406532

TITLE: Fluorescent derivative of NAD in methods of detecting poly(ADP-ribose) polymerase and other NAD-utilizing enzymes

INVENTOR(S): Hergenrother, Paul J.; Putt, Karson S.

PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2005038043	A2	20050428	WO 2004-US34010	20041014
WO 2005038043	A3	20050707		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,			

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

US 20070078100 A1 20070405 US 2006-595360 20061221
PRIORITY APPLN. INFO.: US 2003-510916P P 20031014
WO 2004-US34010 W 20041014

AB The present invention makes use of the discovery that poly(ADP-ribose) polymerase (PARP) and other NAD-utilizing enzymes can be readily detected using a highly sensitive, convenient, simple assay that relies upon the chemical conversion of NAD into a highly fluorescent derivative. NAD conversion is achieved by reaction acetophenone in base (KOH), followed by treatment with acid (formic acid). A simple kit may include NAD solution, 88% formic acid, 2M KOH, 20% acetophenone (in EtOH) solution, a suitable enzyme assay buffer, and suitable control reagents. The assay may also detect genetic deficiencies involving NAD-utilizing enzymes, such as long-chain 3-hydroxyacyl-CoA dehydrogenase.

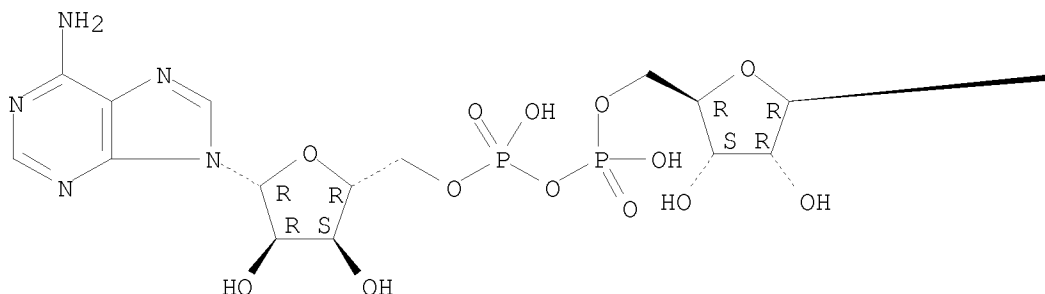
IT 679842-11-6P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(fluorescent derivative of NAD in methods of detecting poly(ADP-ribose) polymerase and other NAD-utilizing enzymes)

RN 679842-11-6 CAPLUS

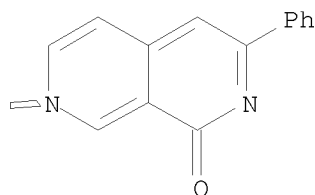
CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with
3-phenyl-7-β-D-ribofuranosyl-2,7-naphthyridin-1(7H)-one (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:109240 CAPLUS

DOCUMENT NUMBER: 140:334458

TITLE: An enzymatic assay for poly(ADP-ribose) polymerase-1 (PARP-1) via the chemical quantitation of NAD+: application to the high-throughput screening of small molecules as potential inhibitors

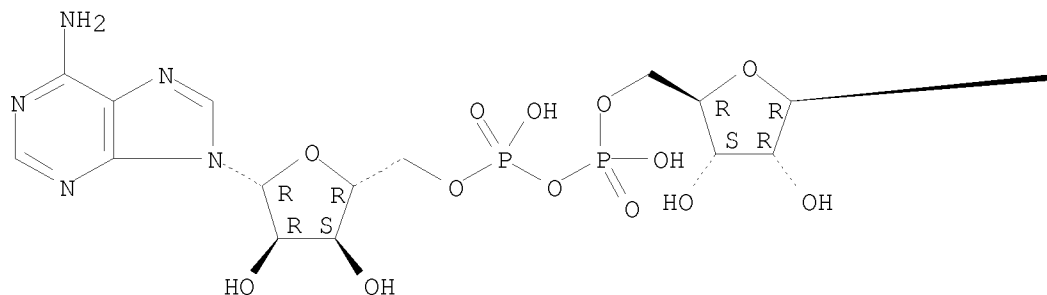
AUTHOR(S): Putt, Karson S.; Hergenrother, Paul J.
 CORPORATE SOURCE: Department of Biochemistry, University of Illinois,
 Urbana, IL, 61801, USA
 SOURCE: Analytical Biochemistry (2004), 326(1), 78-86
 CODEN: ANBCA2; ISSN: 0003-2697
 PUBLISHER: Elsevier Science
 DOCUMENT TYPE: Journal
 LANGUAGE: English

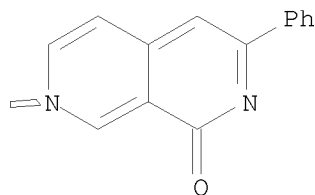
AB The enzyme poly(ADP-ribose) polymerase (PARP-1) catalyzes the formation of (ADP)-ribose polymers on a variety of protein acceptors in a NAD⁺-dependent manner. While PARP-1 is activated by DNA damage and plays a critical role in cellular survival mechanisms, its overactivation leads to a depletion of NAD⁺/ATP energy stores and ultimately to necrotic cell death. Due to this dual role of PARP in the cell, small-mol. inhibitors of the PARP family of enzymes have been widely investigated for use as potentiators of anticancer therapies and as inhibitors of neurodegeneration and ischemic injuries. Unfortunately, standard assays for PARP inhibition are not optimal for the high-throughput screening of compound collections or combinatorial libraries. Described herein is a highly sensitive, inexpensive, and operationally simple assay for the rapid assessment of PARP activity that relies on the conversion of NAD⁺ into a highly fluorescent compound. We demonstrate that this assay can readily detect PARP inhibitors in a high-throughput screen using 384-well plates. In addition, the assay can be used to determine IC₅₀ values for PARP inhibitors that have a range of inhibitory properties. As existing PARP assays utilize specialized reagents such as radiolabeled/biotinylated NAD⁺ or antibodies to poly(ADP-ribose), the chemical quantitation method described herein offers a highly sensitive and convenient alternative for rapidly screening compound collections for PARP inhibition.

IT 679842-11-6
 RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
 (NAD⁺-acetophenone reaction product; high-throughput screening for poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors via the chemical quantitation of NAD⁺)
 RN 679842-11-6 CAPLUS
 CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with 3-phenyl-7-β-D-ribofuranosyl-2,7-naphthyridin-1(7H)-one (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1982:558597 CAPLUS

DOCUMENT NUMBER: 97:158597

ORIGINAL REFERENCE NO.: 97:26381a,26384a

TITLE: Studies of covalent adducts of NAD(P) and enolizable ketones as specific glutamate dehydrogenase inhibitors

AUTHOR(S): Marchand, Jean; Torreilles, Jean; Guerin, Marie Christine; Descomps, Bernard; Crastes de Paulet, Andre; Gabriel, Marc; Larcher, Dominique

CORPORATE SOURCE: INSERM, Montpellier, 34100, Fr.

SOURCE: Biochimie (1982), 64(3), 203-9

CODEN: BICMBE; ISSN: 0300-9084

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Structural analogs of NADH or NADPH of dehydrogenases are prepared by addition of carbonyl compds., including pyruvate, α -oxoglutarate, oxalacetate, butyraldehyde, acetaldehyde, and acetone, to the oxidized coenzymes NAD(P). Some of the adducts obtained are specific inhibitors of glutamate dehydrogenase. The specificity is related to the carbonyl compound used. The high sensitivity of the dehydrogenases for adducts is evidenced by inhibition studies with NAD(P)-pyruvate and NAD(P)- α -oxoglutarate adducts on both activities of glutamate dehydrogenase. The inhibitions are competitive with the reduced coenzymes and the oxidized substrate. Thus, the adducts may be considered as structures closely related to the ternary complexes of the dehydrogenase.

IT 72506-97-9 81793-86-4 81793-87-5
81793-88-6

RL: BIOL (Biological study)

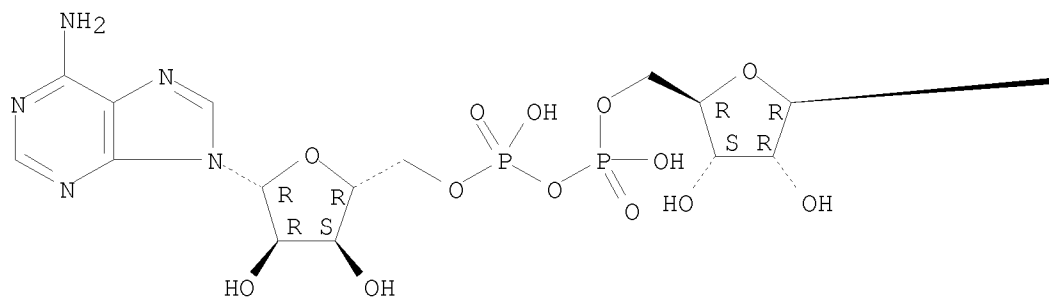
(glutamate dehydrogenase inhibition by, specificity of)

RN 72506-97-9 CAPLUS

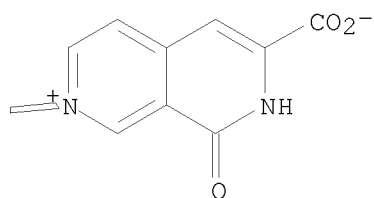
CN Adenosine 5'-(trihydrogen diphosphate), P' \rightarrow 5'-ester with 6-carboxy-7,8-dihydro-8-oxo-2- β -D-ribofuranosyl-2,7-naphthyridinium, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



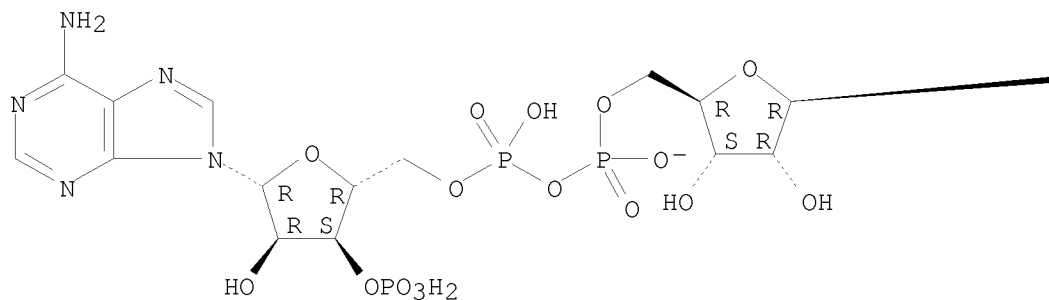
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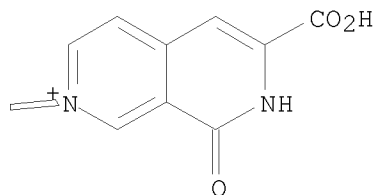
RN 81793-86-4 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate), 3'-(dihydrogen phosphate),
P'→5'-ester with 6-carboxy-7,8-dihydro-8-oxo-2-β-D-
ribofuranosyl-2,7-naphthyridinium, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

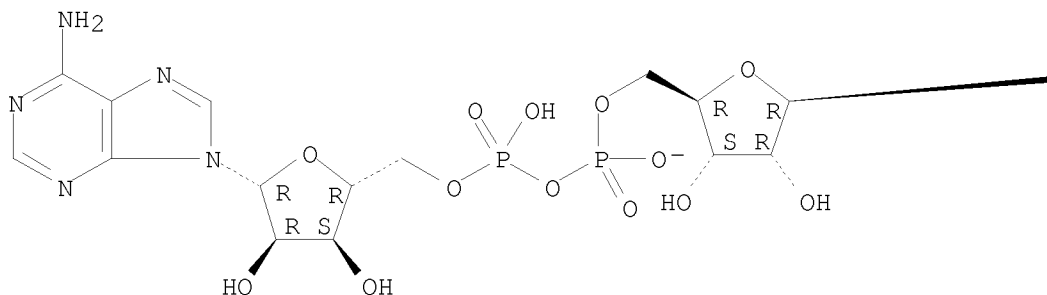


RN 81793-87-5 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with

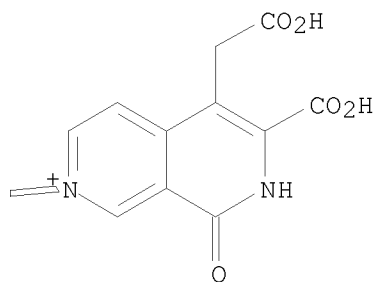
6-carboxy-5-(carboxymethyl)-7,8-dihydro-8-oxo-2,7-naphthyridinium inner
salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



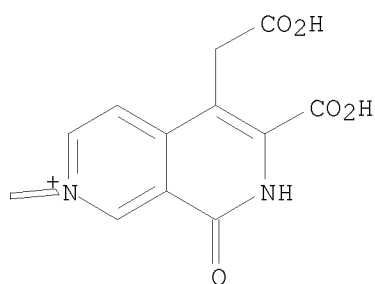
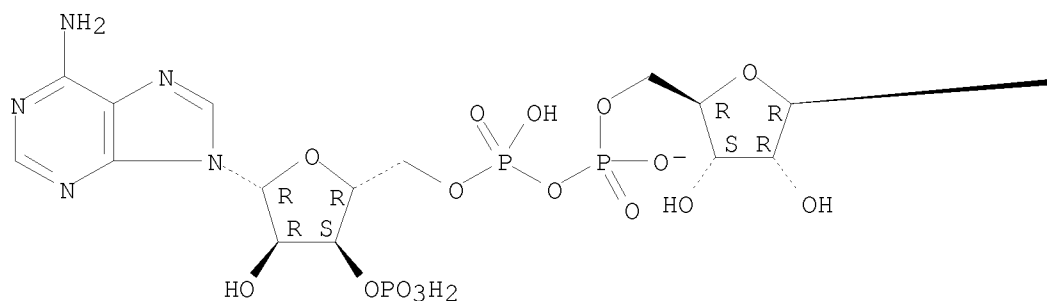
PAGE 1-B



RN 81793-88-6 CAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 3'-(dihydrogen phosphate),
P'→5'-ester with 6-carboxy-5-(carboxymethyl)-7,8-dihydro-8-oxo-2-
β-D-ribofuranosyl-2,7-naphthyridinium, inner salt (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1980:53567 CAPLUS

DOCUMENT NUMBER: 92:53567

ORIGINAL REFERENCE NO.: 92:8827a,8830a

TITLE: Acid-base equilibriums of the oxidized
 β -nicotinamide adenine dinucleotide-pyruvate
 adduct in the ground and electronically excited
 states. A proton transfer probe for proteins

AUTHOR(S): Gafni, Ari

CORPORATE SOURCE: Chem. Phys. Dep., Weizmann Inst. Sci., Rehovot, Israel

SOURCE: Biochemistry (1980), 19(1), 237-44

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Proton transfer reactions of the oxidized NAD-pyruvate adduct in its electronically excited singlet state were studied in aqueous solution and when bound to several proteins. The ionization constant of the adduct in the excited state differed by several orders of magnitude from its value in the ground state. A rapid deprotonation reaction followed electronic excitation if a suitable proton acceptor was present. The deprotonation was accompanied by a marked change in the fluorescence spectrum of the adduct and was therefore easy to detect and follow. The free adduct in aqueous solution was in equilibrium between open and folded conformations of which only the open one was fluorescent. The equilibrium constant between these 2

forms was evaluated. A complex dependence of the fluorescence on the pH in the range of 1-7 was found, which originates in a shift of the equilibrium constant toward the open conformation and in protonation of acid groups of the adduct. Interaction of the adduct with 4 proteins was studied. Each had a different effect on the proton transfer reaction, reflecting differences in the microenvironment of the bound adduct. A possible use of the adduct as an excited-state proton transfer probe for proteins is presented.

IT 72506-97-9

RL: PRP (Properties)

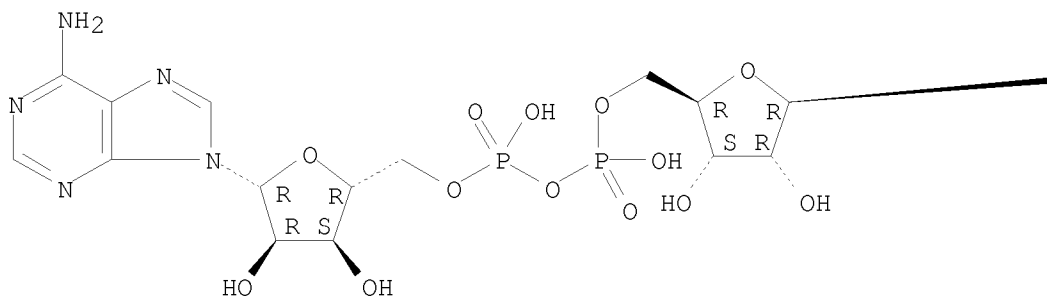
(acid-base equilibrium of, protein effect on)

RN 72506-97-9 CAPLUS

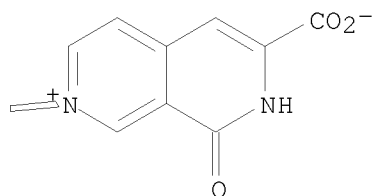
CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with
6-carboxy-7,8-dihydro-8-oxo-2-β-D-ribofuranosyl-2,7-naphthyridinium,
inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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